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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,925	03/11/2004	Glenn Kawasaki	NATH-003	6828

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EXAMINER	
SHIN, DANA H	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/799,925	KAWASAKI ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 32-38* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 7-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,6,18-23 and 32-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on November 27, 2006.

Currently, claims 1-23 and 32-38 are pending. Claims 2-4 and 7-17 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim, as indicated in the previous Office action. Applicants have added claims 32-38, all of which are drawn to an elected invention.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This application contains claims 2-4 and 7-17 drawn to an invention nonelected with traverse in the reply filed on May 31, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 103

Claims 1, 5-6, and 18-23 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hsuih et al. (*Journal of Clinical Microbiology,* 1996) and Wenz et al. (US 2003/0119004 A1) in view of Hannon (*Nature,* 2002) for the reasons of record as set forth in the Office action mailed on July 27, 2006 and for the reasons stated below.

Applicant's arguments filed on November 27, 2006 have been fully considered but they are not persuasive. Contrary to applicant's assertion that there is no motivation to combine the prior art teachings and that the claimed invention is not obvious, it is found that the claimed invention taken as a whole would have been obvious over the combined teachings of the prior art for the reasons state in the previous Office action and set forth below.

First, as applicant has pointed out, Wenz et al. do not explicitly disclose the term "siRNA". Nevertheless, the disclosure of Wenz et al. (see paragraphs 0061-0062) corresponds to the description of the claimed subject matter "target nucleic acid" disclosed in the instant application. On page 8 of the instant application, it is clearly stated that "the target nucleic acid is a RNA that does not exceed about 30 nt" and that it "may be single-stranded or double-stranded". In line with the specification, Wenz et al. expressly teach that the target nucleic acid sequence may be DNA or RNA, either single-stranded or double-stranded.

Second, the two references by Hsuih et al. and Wenz et al. teach methods of quantifying the amount of target nucleic acid in a sample by contacting the sample with at least two oligonucleotides that adjacently hybridize to said target nucleic acid, whereby the resultant pseudotarget nucleic acid is amplified via PCR and quantified. See Abstract and Figure 2 of Shuih et al. and paragraphs 0062, 0123-0126, 0230, 0268, and Figures 1, 12-13 of Wenz et al.

Third, as applicant has pointed out, neither Hsuih et al. nor Wenz et al. teach the specific length limitations (e.g., less than 30 nt) of the target nucleic acid. However, the review article of Hannon teaches that double-stranded RNA (dsRNA) is processed to about 21 to 25 nucleotide RNAs, which are called siRNAs in the art (see page 245). Further, Hannon teaches that Dicer enzyme required for RNAi generates about 22 or about 21-23 nucleotide RNAs (see page 245, and Figures 2 and 4). Along with the term "siRNA", Hannon also introduces the term "shRNA", which mediates RNAi gene silencing (page 250).

In summary, the deficiency present in the teachings of Hsuih et al. and Wenz et al. is the lack of length limitations of the target nucleic acid specifically recited in the instant claims, namely "less than about 30 nt" or "not to exceed about 25 nt", which are characteristic of siRNAs (or shRNAs). However, Hannon's review article clearly teaches the concept of RNA interference (RNAi) and the genome-wide and therapeutic utility of siRNA/shRNA. For example, Hannon teaches that shRNAs will be useful for large scale loss-of-function genetic screens and RNAi-based therapeutics (page 250).

The advantages of the quantifying method of Hsuih et al. is the increased specificity and accuracy of quantification of a target nucleic acid (pages 501 and 505-506). The practical utility of the ligation/amplification quantifying method of Wenz et al. encompasses gene expression profiling and screening/detecting the amount of disease-associated mRNA (paragraphs 0116-0119).

In view of the foregoing, it would have been obvious to one of ordinary skill in the art to use the quantifying methods of Hsuih et al. and Wenz et al. for siRNA or shRNA of Hannon, by replacing the long-stranded target nucleic acids of Hsuih et al. and Wenz et al. with the short, double-stranded target nucleic acids of Hannon. The skilled artisan would have been motivated

to quantify the amount of siRNA/shRNA that is less than 25 nucleotides in length in a sample by adopting the methods of Hsuih et al. and Wenz et al. because siRNA/shRNA is a rapidly growing interest in the current state of the art for their potent inhibitory functions, and therefore the skilled artisan would have been motivated to devise a method of detecting the amount of the newly emerged nucleic acid, siRNA/shRNA. Since Hsuih et al. teach that their quantifying method is specific and accurate and since Wenz et al. teach that their quantifying method can be used in the clinical areas of screening/detecting/diagnosing, the skilled artisan would have been further motivated to utilize the methods of Hsuih et al. and Wenz et al. to detect the amount of siRNA/shRNA administered to patients undergoing RNAi-based therapeutics as taught by Hannon (page 250), thereby monitoring the level of siRNA/shRNA agent in the patients. In conclusion, it would have been *prima facie* obvious to combine the teachings of the accuracy of Hsuih et al.'s method, the clinical application of Wenz et al.'s method, and the RNAi-mediated therapeutics comprising siRNA/shRNA of Hannon, thereby arriving at the instantly claimed invention.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 32-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hsuih et al. (*Journal of Clinical Microbiology,* 1996) and Wenz et al. (US 2003/0119004 A1) in view of Hannon (*Nature,* 2002). Note that the claims are newly entered and that this rejection is necessitated by the claim amendments entered after the non-final rejection.

Claims are drawn to a method of quantifying a target nucleic acid/siRNA duplex, wherein the target nucleic acid ranges in length from about 20 to about 23 nt and wherein the siRNA duplex ranges in length from about 15-30bp, 20-29bp, and 21-23bp.

As stated above, both Hsuih et al. and Wenz et al. teach methods of quantifying a target nucleic acid in a sample, wherein the sample is RNA or DNA or double-stranded DNA. Neither Hsuih et al. nor Wenz et al. teach methods of quantifying a nucleic acid sample, wherein the sample is a short interfering RNA (siRNA).

Hannon teaches the siRNA structure, in particular, ranges of siRNA length: about 21 to 25, about 22, or about 21 to 23. See page 245 and Figures 2 and 4. Hannon also teaches that shRNA mediates RNA interference (RNAi). See page 250.

It would have been obvious to one of ordinary skill in the art to use the methods of quantifying a target nucleic acid in a sample of Hsuih et al. and Wenz et al. in order to quantify

the siRNA or shRNA of Hannon. The structural hallmark of siRNA or shRNA is the short length, which does not exceed 25 nucleotides as taught by Hannon. The various length limitations of siRNA/shRNA claimed in the instant claims are therefore *prima facie* obvious, because the instantly set forth limitations are art-recognized innate and inherent properties of siRNA/shRNA. Again, the skilled artisan would have been further motivated to utilize the methods of Hsuih et al. and Wenz et al. to detect the amount of siRNA/shRNA (ranges in length 20-23 bp) administered to patients undergoing RNAi-based therapeutics as taught by Hannon (page 250), thereby monitoring the level of siRNA/shRNA agent in the patients. In conclusion, it would have been *prima facie* obvious to combine the teachings of the accuracy of Hsuih et al.'s method, the clinical application of Wenz et al.'s method, and the RNAi-mediated therapeutics comprising siRNA/shRNA of Hannon, thereby arriving at the instantly claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635